REMARKS

Claims 1-17, 51 and 52 are pending in the case and all have been rejected.

Claim Objections

Claims 2, 4-8, 10 and 51 were objected to due to the inclusion of non-elected subject matter in that they cover sequences in addition to those elected for examination of the combination claims of Group I. In response, claim 2 has been amended to recite the 10 sequences previously elected.

Claim 8 was objected to for double use of the word "cell" in the claim. In response, claim 8 has been amended to remove this error.

Claim 51 was amended to remove identification of sequences.

Objection to the Specification

The specification was objected to because of the typographical error at page 9, line 24, of the application. In response, Applicants have amended the specification to delete the phrase "1-1-92" and replace it with "1-92" meaning sequences 1 to 92. Applicants believe this correction merely avoids confusion and adds no new matter.

Rejection Under 35 U.S.C. §112 (First Paragraph)

Claims 1-17, 51 and 52 were rejected under 35 U.S.C. 112, first paragraph, as failing to meet the written description requirement due to open claim language such as

"containing a gene that corresponds to a polynucleotide" (claim 1) and "comprising a nucleotide sequence corresponding to a gene" (claim 52).

Applicants respond that this cannot be based solely on use of open ended language because such language as "comprising" is standard claim language and such a rejection could therefor be applied to almost every patent claim. Thus, this rejection must be predicated on use of the term "corresponding" in conjunction with "comprising."

Applicants direct the Examiner's attention to the application at page 11, lines 27-31, where the term "correspond" is defined as meaning a gene that encodes an RNA at least 90% identical to the claimed polynucleotide, which could include an RNA pre- or post-processing (see application at page 12, lines 11-25). In essence, the term "correspond" is intended to indicate polynucleotides that encode substantially the same RNA as a gene in a cell because the disclosed polynucleotides of the application are cDNAs while the genes contained in cells used for the screening process of claim 1 will commonly be genomic sequences contained in cancerous or normal cells as recited in the claim (or may be cDNAs transfected into recombinant cells used for screening). For example, such a polynucleotide would encode the same protein as the gene it corresponds to in the case where the gene encodes a protein (see application at page 13, lines 6-14).

In addition, Applicants note that the methods of claims 1 and 52 relate to contacting a cell with a test compound to be evaluated for gene modulating ability. The gene to be modulated is therefor contained in the cell used in the screen and such gene may certainly be part of the genome of said cell, in which case it will be part of a larger polynucleotide structure. Thus, the cell comprises the gene.

Further, the sequences disclosed by Applicants are mostly cDNA sequences so that they mostly result from processed RNA species from which intronic sequences have been removed. For this reason it would avail Applicants little to identify the gene as

comprising one of the disclosed sequences since such cDNA sequence, as such, would not be contained within the cell. In addition, gene expression is normally determined by measuring RNA expression and the structure of the RNA therefor corresponds to both the gene expressing it as well as the cDNA that would be formed from it. Consequently, the gene of the cell and the polynucleotide disclosed by Applicants correspond to each other through the RNA that is related to both. As a result, Applicants define the term "correspond" as in the application at page 11, lines 27-31, as meaning a gene that encodes an RNA at least 90% identical to the claimed polynucleotide, which is commonly a cDNA sequence, and could include an RNA pre- or post-processing (as stated in the application at page 12, lines 11-25).

In sum, a user of a method of the invention may well use a cell that contains the genomic counterpart of a polynucleotide (such as a cDNA sequence) disclosed by Applicants and thus it would be expression of the genomic counterpart of Applicant's polynucleotide that is being measured. However, such would readily be recognized by those skilled in the art and therefor in no way detracts from the patentability of the invention as recited in claims 1 and 52 (and claims dependent therefrom).

In view of the foregoing, Applicants believe that the written description requirement has been met by the application disclosure as filed and thus clai 1 and 52, and claims dependent therefrom, should be allowed.

Rejection Under 35 U.S.C. §112 (Second Paragraph)

Claims 1-17, 51 and 52 were rejected as vague and indefinite for use of the term "corresponds" and "corresponding."

Claim 52 was rejected as vague for use of the phrase "a polynucleotide comprising a nucleotide sequence corresponding to a gene." Applicants respond by reiterating the

above-description of the term "correspond" and note that the indicated phrase merely refers to the fact that the polynucleotide used for screening is contained in a cell as recited in the claim and therefore may be part of the genome of the cell, thus being part of a larger polynucleotide structure. Thus the cell would contain a polynucleotide capable of modulation and the sequence of the polynucleotide would correspond to one of the genes disclosed in the application as exhibiting increased expression in a cancerous versus a non-cancerous cell or vice versa. Applicants believe that this recitation is sufficiently clear to avoid any argument for vagueness.

Claims 1 and 54 were rejected as vague for use of "corresponding" in the phrase "a polynucleotide comprising a nucleotide sequence corresponding to a gene." Applicant responds by reiterating the above-description of the term "correspond" and note that the indicated phrase merely refers to the fact that the polynucleotide used for screening is contained in a cell as recited in the claim and therefore may be part of the genome of the cell, thus being part of a larger polynucleotide structure. Thus the cell would contain a gene capable of modulation and the sequence of the gene would correspond to one of the polynucleotides disclosed in the application as exhibiting increased expression in a cancerous versus a non-cancerous cell or vice versa. Applicant believes that this recitation is sufficiently clear to avoid any argument for vagueness.

Claims 1 and 52 were rejected as indefinite for use of the terms increase and decrease and elevated. Applicants note that the application indicates the observed changes in expression for the different ranges of SEQ ID NOs disclosed in the application. Further, applicants believe that those skilled in the art are well capable of determining whether a change in gene expression due to the presence of a potential therapeutic agent is reliable or not. Applicants also note that the invention is directed to determining the effects of chemical agents on the expression of more than one gene in cancerous versus non-cancerous cells or vice versa and that it is the overall profile of gene modulation that is relied on in determining the agent in question and not the absolute change in expression of any particular gene.

Claims 1 and 52 were also rejected as indefinite for use of the phrase "cancerous cell over that in a non-cancerous cell" etc. In response, Applicants have amended the claims to recite that the cells are from the same tissue type. This amendment is supported in the application, for example at page 20, lines 25-30.

Claims 1 and 52 were rejected as indefinite for use of the phrase "under conditions" and, in response, Applicants have amended these claims to delete this phrase and, instead, recite that the indicated gene is being expressed.

Claim 15 was rejected as indefinite for use of the term "first" to denote that the compound used in the method of claim 15 was not previously known to have gene modulating activity and was first identified as such using the method of claim 1. In response, Applicants have amended this claim to recite more extensive language.

Rejection Under 35 U.S.C. §102

Claims 1-17, 51 and 52 were rejected under 35 U.S.C. 102(e) as anticipated by Young et al (WO 01/94629).

In response, Applicants contend that Young et al does not meet the requirements of 102(e) as a reference as of its filing date because it does not designate the United States as a designated state (see face page of the published application of Young et al).

In view of the foregoing, Applicants believe that this ground of rejection has been overcome.

R jection Under 35 U.S.C. §103(a)

Claims 1-17, 51 and 52 were rejected under 35 U.S.C. §103(a) as being unpatentable over Robinson et al. (Pat. No. 6,232,065) in view of a number of GenBank Accession Nos., Young et al. (WO 01/94629) and Kinzler et al. (Pat. No. 5,702, 903).

Robinson et al. is offered as a basis of rejection on grounds that this patent discloses methods and compositions for screening factors that affect the expression patterns of individual genes or groups of genes in various disease states, including colon cancer, and also examining an entire gene family profile to identify important marker genes for subsequent experiments to identify cancer and other cancer-related testing. In addition, Robinson et al is cited as describing many of the multiple genes showing expression changes in a particular tyrosine kinase gene family. However, the Examiner concedes that Robinson et al do not describe the use of squamous carcinoma cells, decreases in neoplastic activity due to cell death or the particular sequences disclosed by Applicants.

The Examiner attempts to make up for the latter deficiencies by relying on Young et al. However, because of the effective date of Young et al (i.e., its publication date) as well as the other comments already made by Applicants, this reference has been removed and will thus not be described further.

The Examiner also relies on Kinzler et al to bolster the case for obviousness. This reference is relied on to show elevated gene expression in various tumors, such as those from stomach, lung and colorectal cancer, as well as describing elevated expression over that normally produced in non-cancerous cells.

In response, Applicants contend that Kinzler et al merely use the normal cells to establish baseline expression levels (see Kinzler at column 5, lines 60-63). However, there is no mention of the sequences disclosed by Applicants as being involved in the cancerous process. The sequences and genes disclosed by Applicants herein were not

previously known as being involved in the cancerous process, especially not when taken as a group or family (such as the signature gene sets disclosed by Applicants). It is the identity of the sequences in conjunction with their differential expression as a group (or, at least, as more than one gene) and uses thereof that forms a basis for the present invention. The mere fact that the sequences were previously known or that someone skilled in the art had previously disclosed use of differential expression of a gene for screening potential therapeutic agents in no way negatives patentability of the present invention.

At best, Kinzler et al. and Robinson et al. taken together merely tell those in the art to go out and look for genes and/or groups of genes. However, they do not render obvious the Applicant's claimed method since this involves specific sequences found by the Applicant as part of a larger profile.

The Examiner further relies on Robinson et al as teaching the monitoring of gene expression profiles resulting from cellular and physiological changes that can then be characterized for individual genes or groups of genes. Robinson further states that the invention can be used to screen drug compounds that affect biological samples and that human cancer is a result of genetic changes that result in alterations in the profile of expressed genes. The Examiner suggests that this method could be applied by combining the disclosures of Young et al and Kinzler et al to check for the presence of gene expression alterations involved in normal and cancerous tissue in order to find compounds that alter the differential expression between cancerous and non-cancerous cells.

In response Applicants contend that these references, if combined, do not achieve the invention of the application. The Applicants concede that all of their disclosed sequences were already known in the art but not as being up-regulated in cancerous versus non-cancerous cells or vice versa. The Examiner cites accession numbers and references for sequences with high similarity or identity to 10 of the sequences disclosed

by Applicant.

None of the references appear to recite use of genes elevated in normal cells as opposed to cancer cells although this is within the scope of claim 1 and is specifically required by claim 51. For example, Kinzler et al. uses non-cancerous cells to develop a baseline for elevated gene expression in cancerous cells but does not assess elevated production in normal cells versus cancerous cells (see Kinzler et al. at column 5, lines 60-67). In fact, several of the gene sequences provided by Applicant in the selected 10 sequences are elevated in normal over cancerous cells (for example, SEQ ID NO: 851, 1979 and 2032 are expressed in normal and not cancerous tissues of lung while SEQ ID NO: 995, 1021, 1062, 1300, 1340, 1483 and 1549 are expressed in carcinoma of the lung but not in normal lung tissues).

Applicant believes that this is an application of the "obvious to try" standard, which is not sufficient to show prima facie obviousness. (See, for example, In re Eli Lilly & C., 14 USPQ2d 1741, at 1743 (Fed. Cir. 1990), where this is defined as a general disclosure that "may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions were pursued.") In the present case, Applicant does not believe that a mention of finding a gene with differential expression in a cancer cell tells those skilled in the art to look for families of such genes, or determined expression profiles of such families, or to examine elevated expression in normal over cancerous cells or the particular sequences disclosed by Applicant (especially since Young et al is not a reference).

Additional Claim Amendments

Claims 4, 6, 7, 8, 10 and 51 have been amended to remove sequence number identifications.

Claim 11 has been amended to recite use of at least 3 said genes. Support for this amendment is found in the application at page 10, line 3, and at page 18, lines 3-8.

Claim 14 has been amended to recite use of more than 10 said genes. Support for this amendment is found in the application at page 10, line 5.

Further, claim 51 was amended to recite the method of claim 1 wherein at least one gene is a gene elevated in cancer and not in normal cells and at least one gene is elevated in normal cells and not in cancer cells. For example, genes corresponding to 3 of the 10 sequences previously selected have been found to be expressed in normal but not cancer cells while genes corresponding to 7 of the selected sequences are expressed in cancer cells but not normal cells.

As a final matter, Applicants note that a paper was included with the Office Action indicating that Applicant must comply with the sequence rules, noting an election of Group IV and signed by an Examiner Fredman. Applicants' agent telephoned the Examiner herein and confirmed that this paper was forwarded by error. Thus, no response is being made to said paper.

Applicants have included herewith a request for a 2 month extension of time and the fee paid by enclosed check. The Commissioner is authorized to charge payment of any additional fees required for filing this response, or credit any overpayment, to Deposit Account No. 03-0678.

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Respectfully submitted,

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